

## REMARKS

Claims 1 and 9 were pending. In the Office Action of February 29, the Examiner rejected claims 1 and 9. Applicants have not amended or cancelled any claims herein. Applicants have added new claim 19; support for the new claim can be found at paragraph [0047] of the U.S. Publication of the present case, U.S. 2005/0272750. No new matter has been added. Accordingly, claims 1, 9, and 19 are pending.

In light of the remarks herein, Applicants respectfully request reconsideration and allowance of the pending claims.

### Rejections under 35 U.S.C. § 103

The Examiner rejected claims 1 and 9 under 35 U.S.C. § 103(a) as being obvious over Willis *et al.* (WO 01/25242, US 6,790,850) (hereinafter "Willis"). In particular, the Examiner asserted that the presently claimed compound was an adjacent homolog of a species found in claim 4 of Willis, namely the species 5-[[2,3-difluorophenyl)methyl]thio]-7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]thiazolo[4,5-d]pyrimidin-2(3H)-one, and alleged that an adjacent homolog was generally of sufficiently close structural similarity to the Willis species that there was a presumption that the presently claimed compound would possess similar properties as the Willis compound. In addition, the Examiner rejected Applicants' prior assertions, including evidence submitted in a Declaration under 37 C.F.R. § 1.132, that the presently claimed compound, a *particular stereoisomer* having 2 stereocenters in the *S* configuration, namely 5-[[[(2,3-difluorophenyl)methyl]thio]-7-{{*(1S,2S)*-2-hydroxy-1-(hydroxymethyl)-propyl]amino}thiazolo[4,5-d]pyrimidin-2(3H)-one, was not an obvious variant of the Willis compound.

The Supreme Court recently clarified that for an invention to be obvious under § 103 requires consideration of the factors set forth in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), including an analysis of the scope and content of the prior art and the differences between the claimed subject matter and the prior art. See *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. \_\_\_\_ (2007), 127 S. Ct. 1727 (hereinafter "KSR"). However, as the Federal Circuit recently

clarified in *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1363 (Fed. Cir. 2007), and *Eisai Co. Ltd. v. Dr. Reddy's Laboratories, Ltd.*, 2008 WL 2791884 (Fed. Cir. July 2008) (copies attached), in order to assert that a compound is obvious over a compound in the prior art, one must: 1) identify a starting reference point or points in the art (*i.e.*, a lead compound), prior to the time of invention, from which a skilled artisan might identify a problem and pursue a potential solution; 2) identify some reason, available within the knowledge of one of skill in the art, to make the *specific molecular modifications* necessary to result in the claimed compound; and 3) identify “some reasons for narrowing the prior art universe to a finite number of identified, predictable solutions.” Importantly, in an unpredictable art such as chemistry, *Eisai* confirmed that *KSR*'s focus on “identified, predictable solutions” may present a difficult hurdle because of the genuine unpredictability of the art. Indeed, in *Eisai* the Federal Circuit stated “[i]n other words, post-*KSR*, a *prima facie* case of obviousness for a chemical compound still, in general, begins with the reasoned identification of a lead compound.”

Here, the Examiner has failed to identify a reason why one having ordinary skill in the art would make the presently claimed compound given the cited Willis art. In particular, Applicants assert that the Examiner has failed to satisfy the requirements set forth in *Takeda* and *Eisai* for establishing a *prima facie* case of obviousness of a chemical compound. First, the Examiner has failed to make a reasoned identification of a lead compound in the Willis reference. Although the Examiner asserts that the presently claimed compound is an adjacent homolog of a species in Willis, the Examiner provides no reason why one having ordinary skill in the art would pick the Willis compound 5-[[2,3-difluorophenyl)methyl)thio]-7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]thiazolo[4,5-d]pyrimidin-2(3H)-one as a lead compound. There is simply nothing in the Willis reference to point to this compound as a lead compound. Applicants note that the Willis reference discloses a genus of compounds that encompasses a large number of compounds. In fact, 48 specific compounds are exemplified in the Willis reference, with an additional 5 sodium salts and 6 other salts of particular compounds exemplified. Accordingly, since the homologous Willis compound has not been reasonably identified as a lead compound, the Examiner has not further identified any reason why one having ordinary skill in the art would then have *any* motivation to make an adjacent homolog of this particular Willis compound at that particular position, given the large number of other compounds encompassed by the genus and

the 47 other compounds exemplified, let alone one having the particular stereochemistry of the claimed compound. Clearly the Examiner cannot be asserting that every possible compound of the genus and the 48 particular species set forth in the Willis reference could be a lead compound, and thus that every possible homolog and stereoisomer at every possible position is *prima facie* obvious over the Willis reference. Since the Examiner has failed to establish a *prima facie* case of obviousness over the Willis reference according to the standards set forth in *Takeda* and *Eisai*, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103.

#### Double Patenting Rejections

The Examiner rejected claim 1 and 9 on the ground of non-statutory obviousness-type double patenting over claims 1-11 of U.S. Patent 6,790,850 (the Willis reference discussed above). The Examiner also provisionally rejected claims 1 and 9 on the ground of non-statutory obviousness-type double patenting over claims 20-26 of co-pending application 10/863995, a continuation application of the Willis reference. In both cases, the Examiner asserted that the claimed homologous Willis species 5-[[2,3-difluorophenyl)methyl]thio]-7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]thiazolo[4,5-d]pyrimidin-2(3H)-one rendered the presently claimed compound obvious. Applicants respectfully disagree for the reasons set forth above. Withdrawal of the rejections is respectfully requested.

The Examiner also provisionally rejected claim 1 and 9 on the ground of non-statutory obviousness-type double patenting over claims 1 and 9 of copending application 10/528316, alleging that the sodium salt species recited in claim 1 of the co-pending application was a positional isomer of the presently claimed compound, and that this fact rendered the presently claimed compound obvious. As stated previously, the Examiner has provided no reason for asserting that the co-pending application compound would be identified by one having ordinary skill in the art as a lead compound for modification. Moreover, the Examiner has identified no reason why one having ordinary skill in the art would specifically modify the compound of the co-pending case to result in the presently claimed compound, including, in particular, identifying a reason why one having ordinary skill in the art would modify the co-pending case compound to result in the particular S stereochemistry at the two stereocenters in the presently claimed compound. Indeed, Applicants note that the co-pending '316 is silent as to stereochemistry at

any position, and the Willis reference previously cited by the Examiner exemplifies certain compounds having an R, but not S, stereochemistry at the 1 position.

While the Examiner has asserted the positional isomeric relationship and the frequency of use of a sodium salt as evidence of a *prima facie* case of obviousness, such evidence presupposes the required reasoned identification of a lead compound, which has not been satisfied in the present case. Moreover, while the Examiner points to the Berge reference to support the assertion that sodium is one of the most frequently employed pharmaceutical cations, Applicants note that the Berge reference itself concludes that "selecting a salt form that exhibits the desired combination of properties is a difficult semiempirical choice" and that "only a few generalizations are available to predict the effect of particular salt forms on the characteristics of a drug." Such statements clearly do not support the Examiner's assertions of obviousness, and in fact further bolster the Applicants' rebuttal evidence as set forth in the Declaration under 37 C.F.R. § 1.132, previously submitted. Therefore, Applicants submit that the Examiner has not made out a *prima facie* case of obviousness over the co-pending '316 application. Withdrawal of the rejections is respectfully requested.

Applicant : Brough et al.  
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Filed : March 17, 2005  
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### CONCLUSION

Applicants respectfully assert that all claims are in condition for allowance, which action is hereby requested. The Examiner is invited to telephone the undersigned attorney if such would expedite prosecution.

Please charge Deposit Account No. 06-1050 for the Petition for Extension of Time fee and for the Request for Continued Examination fee. Please apply any other charges or credits to Deposit Account 06-1050.

Respectfully submitted,

Date: 8/29/08

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